

Infective endocarditis with glomerulonephritis associated with cat chlamydia (*C. psittaci*) infection

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SUMMARY A patient with glomerulonephritis and endocarditis is described who had evidence of feline *Chlamydia psittaci* infection. Treatment with antichlamydial drugs resulted in resolution of the glomerulonephritis and the endocarditis. It is recommended that screening for chlamydia is included in the investigation of patients with suspected or obscure endocarditis.

Infective endocarditis is often caused by an unusual organism. The management of such cases is much more effective if the identity of the organism has been established (Friedberg, 1964; Hampton and Harrison, 1967).

We describe a patient with infective endocarditis and secondary glomerulonephritis in whom there was strong evidence of infection with the feline keratoconjunctivitis agent (*Chlamydia psittaci*). This is the first recorded case of endocarditis and glomerulonephritis caused by this organism.

Case report

A 40-year-old man who worked as a steward on a cross-channel ferry was admitted to hospital in December 1976 for investigation of proteinuria. His past illnesses included gonorrhoea in 1972. In May 1976 he developed a pale red-yellow rash over the limbs and trunk with a purpuric component on the legs. This was accompanied by gingivitis, fever, night sweats, and sore throat. Investigations were done in a hospital in Antwerp and showed: Hb 11 g/dl, white cell count $11.8 \times 10^9/l$ (76% lymphocytes), and ESR 83 mm in the first hour. The monospot and Paul-Bunnell test for infectious mononucleosis were negative. The RA latex test was positive and the Rose-Waaler 1/40. $\beta 1A/\beta 1C$ complement was low. IgM was 5.8 g/l (0.38-1.45), IgG was 22 g/l (6-18), and IgA was normal. The blood urea was 9.5 mmol/l (57 mg/dl) and the serum creatinine 185 $\mu\text{mol/l}$ (2.2 mg/dl). Hepatic enzymes were mildly increased but the serum

bilirubin was normal. The urinary protein concentration was 1.6 g/l and the sediment contained numerous red blood cells. Skin biopsy and rectal biopsy showed nonspecific acute vasculitis and liver biopsy a mild nonspecific hepatitis. He was given intramuscular penicillin for 12 days for his gingivitis and also prednisone 20 mg daily for 4 weeks.

In July 1976 in Winchester though generally well, he had lost 2 stones (12.7 kg) in weight. He had the signs of aortic regurgitation not previously recorded but no other evidence of endocarditis. The urine again contained large amounts of protein and blood. Renal function was otherwise normal. Serum complement C3 and C4 were decreased. Chest x-ray and electrocardiogram were normal. The patient was anxious to return to sea and did not reattend until December 1976. At that time he had a urethral discharge. Smears were negative for gonorrhoea and serological tests for syphilis were negative.

He agreed to further investigation in hospital because of increasing exertional dyspnoea over 4 weeks. He had also noted intermittent haematuria and mild night sweats since his illness in May 1976. Physical examination again showed only signs of aortic regurgitation, proteinuria, microscopical haematuria, and casts. His temperature was persistently 38 to 39°C. Investigations showed normochromic anaemia—haemoglobin 8.7 g/dl, white cell count $9.0 \times 10^9/l$, and platelets $267 \times 10^9/l$; ESR was 139 mm in the first hour. The blood urea was 15.0 mmol/l (90 mg/dl) and serum creatinine 175 $\mu\text{mol/l}$ (2.0 mg/dl). The antistreptolysin O titre was 200 IU/ml. Salmonella and brucella agglutinins

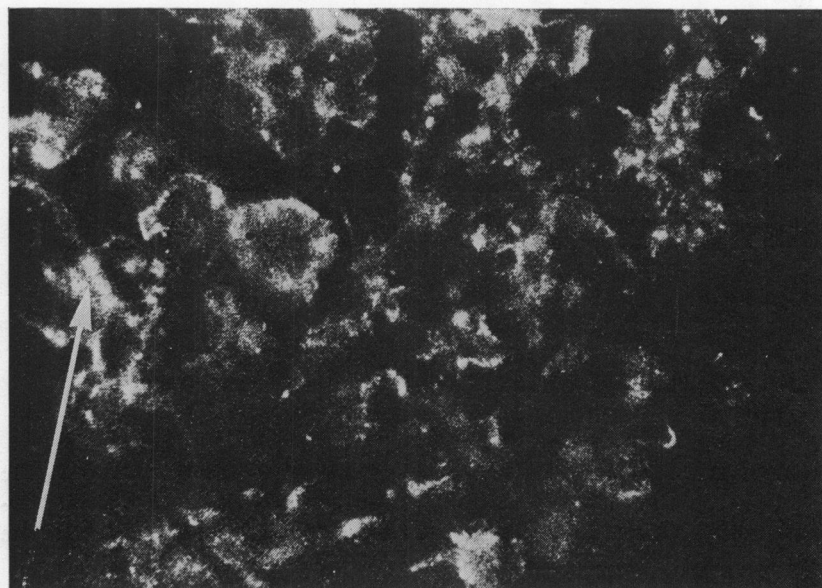


Fig. 1 Glomerulus containing granules of complement (C3) in the capillary walls and mesangium (arrow). IgM is found in a similar distribution. (FITC-swine-antihuman C3 $\times 450$.)

and complement fixation tests were negative as was the Q fever complement fixation test and fungal precipitins. Repeated blood cultures were negative. The RA latex test was negative. Plasma contained type M mitochondrial antibody to a titre of 1/40. Serum complement was decreased C3 at 0.35 g/l (1.0-1.8) and C4 at 0.09 g/l (0.14-0.38). Hepatitis B antigen was negative. Immunoglobulins IgG 28.4 g/l (7-13) and IgM 3.1 g/l (0.4-1.3) were again increased and IgA 2.0 g/l (1.2-3.5) was normal. Sternal marrow aspirate was normal. Renal biopsy showed proliferation of mesangial and endothelial cells and immunofluorescent examination revealed numerous fine granules of IgM and C3 in the basement membranes (Fig. 1).

Eight days after admission the patient experienced the sudden onset of weakness of the left side of his face and body. This resolved rapidly over the next 24 hours. It was thought that he had a cerebral embolus from an infected aortic valve and immediate antibiotic therapy was begun with intravenous penicillin and gentamicin. However, 6 days later he had a further severe left hemiparesis with grossly impaired consciousness. As his fever had still not settled several days later and the cause of the presumed endocarditis was not identified, the antibiotics were changed to ampicillin and clindamycin. Ten days later the psittacosis/lymphogranuloma venereum complement fixation test was $> 1:256$ on plasma taken soon after admission and $> 1:256$ on 2 further specimens. Type specific antichlamydial antibody testing by the modified micro-immuno-

fluorescent method (Treharne *et al.*, 1977) revealed specific antibody against the cat chlamydial type of *C. psittaci* (cat keratoconjunctivitis agent) in titres of IgM 1/64 and IgG 1/1024. In view of this result and the continued spiking fever antichlamydial treatment was begun with erythromycin (tetracycline being avoided because of the renal failure). The temperature returned to normal within 4 days and remained so. Serial measurements of serum complement and creatinine showed both returning to normal (see Fig. 2). Clinical improvement also occurred with return of full consciousness and reversal of weight loss. Despite improvement in the hemiparesis there was some mild persistent intellectual deficit. The ESR returned to normal and the proteinuria and haematuria completely disappeared. Four months after the antichlamydial treatment was begun, antichlamydial antibody levels as measured by the micro-immunofluorescent test had fallen to 1/256 for IgG and less than 1/8 for IgM. Doxycycline was substituted for erythromycin as soon as the patient could reliably take oral medication and will be continued for one year.

Discussion

Although the aetiological agent of this patient's infective endocarditis was not isolated there is serological evidence that the organism responsible was the feline chlamydial agent (feline keratoconjunctivitis agent), a type of *C. psittaci*. The presence of specific antibody (IgM 1/64 and IgG 1/1024)

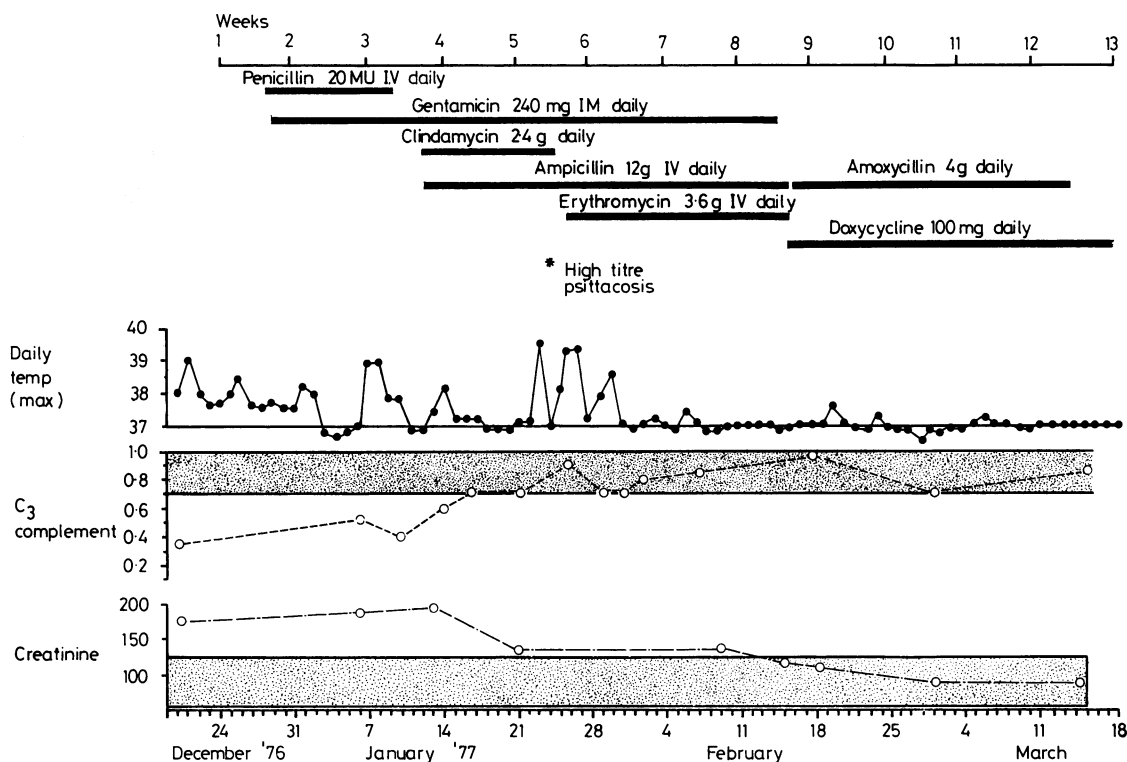


Fig. 2 Serial readings of the patient's temperature, serum complement, and serum creatinine are plotted against time. Antibiotic therapy is also shown. All indices returned to normal.

against cat chlamydia in this patient is highly suggestive of an active infection with this agent. The cat chlamydia agent has previously been shown to cause conjunctivitis in man (Ostler *et al.*, 1969). There have been previous reports of infective endocarditis caused by *C. psittaci* (Levison *et al.*, 1971) (none of those with complicating glomerulonephritis have recovered). However, antichlamydial antibody type-specificity was not determined. Levison described 2 cases and cited several previous reports. Most, but not all, of these patients gave a history of contact with birds. In another study (Ward and Ward, 1974) it was suggested that *C. psittaci* might be aetiologically related to some cases of chronic valvular heart disease. Of 7 patients in whom antigen of *C. psittaci* was identified in the endocardium, 2 had no history of contact with birds. It is possible that in some of these patients the cat chlamydial agent could have been present but *C. psittaci* typing was not done.

Our patient gave a history of prolonged close contact with cats. His fever responded to antichlamydial treatment (erythromycin). After antichlamydial treatment, the level of antichlamydial

IgG and IgM directed against cat keratoconjunctivitis had fallen fourfold or more (from 1/1024 to 1/256 and 1/64 to less than 1/8, respectively). The earlier response of the low C3 complement may have been the result of a partial antichlamydial effect of clindamycin. His proteinuria and haematuria disappeared and the renal function returned to normal on continued antichlamydial treatment with erythromycin followed by doxycycline alone since March 1977. The progress of his aortic regurgitation was arrested from the time of effective treatment of his endocarditis.

The occurrence of glomerulonephritis in association with infective endocarditis is well recognised (Gutman *et al.*, 1972). This nephritis is probably the result of deposition of immune complexes of which the antigen is derived from the infective organism (Levy and Hong, 1973; Perez *et al.*, 1976). One of the patients with endocarditis caused by psittacosis reported by Levison *et al.* (1971) had glomerulonephritis confirmed at necropsy. Our patient had histologically proven glomerulonephritis of which all clinical evidence disappeared on antichlamydial therapy, presumably because of removal

of the antigen. The presence of IgM rather than IgG in the kidney is unusual, but has been noted previously in association with endocarditis (Perez *et al.*, 1976).

This patient appears to be the first in whom the feline keratoconjunctivitis agent type of *C. psittaci* has been implicated in infective endocarditis. He is also the first patient reported whose chlamydial endocarditis was effectively treated with arrest of aortic regurgitation and cure of associated glomerulonephritis.

A history of contact with cats should be sought, along with that of contact with birds, in patients with infective endocarditis where the cause is unclear. A negative history does not exclude the diagnosis. We recommend also that such patients are screened for psittacosis/lymphogranuloma venereum antibody and if positive specific chlamydial typing should be done. Ideally one would like definitive demonstration of the organism. This is unlikely to be achieved at present unless the infected valve should need to be removed.

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Addendum

The patient required aortic and mitral valve replacement for deteriorating left ventricular failure in February 1978. The valves showed no evidence of active endocarditis, but microscopically there

were a few small vegetations. Cultures, including yolk sac culture, were negative, as was electron microscopy. He recovered well postoperatively, but died in another hospital one month later of an acute respiratory illness. Necropsy showed bilateral bronchopneumonia. The prosthetic heart valves appeared normal.

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